REMARKS

The claim dependencies of claims 15, 18 and 20 have been amended to depend from an allowable claim.

Applicants are gratified that claims 10-12, 14, 21-23, 26, 29 and 30 are allowed and claims 25 and 28 are only objected to as dependent on a rejected base claim. Thus, the substance of these claims is indicated allowable.

The only substantive rejection is of claims 24 and 27. Claim 24 is independent and claim 27 is dependent thereon.

Request to Withdraw Finality

First, applicants request that the finality of the rejection be withdrawn since the new rejection is not necessitated by amendment. Claim 24 as previously pending was dependent on claim 23 which was dependent on claim 10. In the Office action mailed 12 October 2010, claim 24 was merely objected to as being dependent on a rejected base claim. (Page 3 of the Office action.) Thus, claim 24 should be in a position for allowance if amended to include all of the limitations of the claims from which it depended. That was in fact done, so the scope of claim 24 has not been changed and thus, the rejection set forth herein was not necessitated by amendment.

In order to demonstrate this, applicants' undersigned representative e-mailed to Examiner Willis on 5 January 2011 a set of claims as they stood and were examined in the Office action mailed 12 October 2010 along with a copy of claim 24 as currently proposed showing where the subject matter from claims 10 and 23 was incorporated so that claim 24 became an independent claim of the same scope as claim 24 as previously dependent on claim 23. Claim 23 defined only R^2. Claim 24 as previously pending defined only R^1, Q, W, A (without defining the various superscripted R's in that definition) and Y, again without such definition. Thus, as shown in the attached, the structure of formula (V) and the definitions of X^1-X^4 from claim 10 were inserted into new claim 24; the definition of R^1 was retained in claim 24; the definition of R^2 was inserted from claim 23; the definition of the superscripted R's in R^2 was inserted from claim 10; the definition of Q and W were as originally set forth in claim 24 and the definitions of the various superscripted R's in the definition of A were inserted from claim 10. The definition of Y was originally in claim 24, but the missing definitions of the superscripted R's were supplied from claim 10.

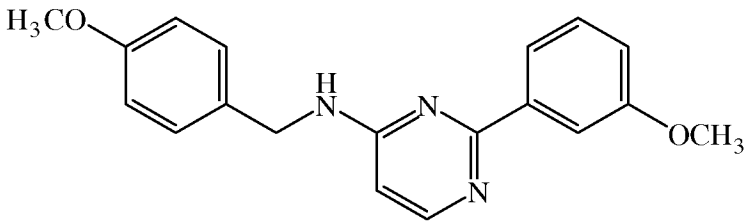
As is evident from the enclosed exhibit, all that was done to claim 24 was to insert the limitations of claims 10 and 23 into it so as to provide it a status as an independent claim. The dates at which these claims were pending is set forth in the lower right-hand corner of the exhibit.

Applicants thus believe that the finality of the rejection should be withdrawn.

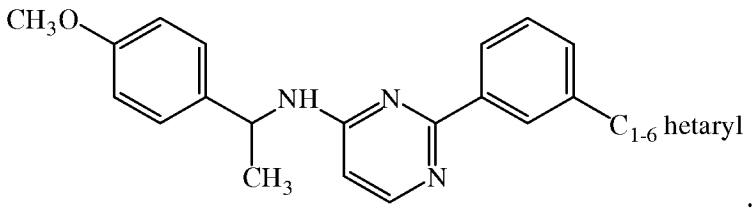
The Rejection Itself

In discussing this with the undersigned by phone on 5 January 2011, Examiner Willis stated that whether the rejection is final or not, the rejection was still one that he wished to maintain. This

rejection is of claims 24 and 27 over Ding, *et al.* (WO03/031406). The rejection states that Ding discloses a compound of the formula:



which, according to the rejection differs from the compounds included in the scope of claim 24 only in that W is -C_{1-4} alkyl and R^2 can be M-C_{1-6} alkylhetaryl. Thus, claim 24 would include compounds of the formula:



This is true. However, applicants believe, as indeed Examiner Willis appears to believe, that C_{1-6} hetaryl is quite different from OCH_3. If applicants understand the rejection correctly, in order to defeat patentability, there must be a document that suggests C_{1-6} hetaryl in the meta position of the phenyl ring shown at the right of the above formula. For this purpose, Yonetoku on page 12, at lines 1-7 is cited.

As page 12 is entirely in Japanese, this appears to be the incorrect citation, and instead, Examiner Willis clarified that it is this location in the Ding document that was intended. Lines 1-7 in Ding state that in formula (XV), R^1 may include phenyl and benzyl substituted on the aromatic ring with a substituent that can include C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} alkyl hydroxy, C_{1-6} alkylamine, C_{1-6} aminoalkyl, halo and heterocycle. Thus, as a first problem, C_{1-6} alkylhetaryl is not listed. Hetaryl and C_{1-6} alkyl containing substituents are listed separately.

Perhaps more important is that in referring to formula (XV) which is set forth on page 10, R^1 is coupled not to the pyrimidine ring, but rather to an aliphatic amine. Thus, R^1 in formula (XV) does not correspond to R^2 in formula (V) set forth in claim 24.

As the disclosure of the possibility of C_{1-6} hetaryl in the position represented by R^2 in the present claims appears to be essential to support the rejection, and as there is no such disclosure in the cited art, this basis for rejection may properly be withdrawn.

As the Examiner phrases it, Ding suggests to replace the OCH_3 at in Ding's substituted pyrimidine compositions with an alternatively useable C_{1-6} alkylhetaryl and it would be obvious replace the H at W in Ding's compositions with an alternatively useful $-CH_3$.

While applicants do not agree that replacing the H at W with CH_3 is necessarily obvious in all cases, this need not be argued as Ding clearly does not suggest replacing OCH_3 with C_{1-6} alkylhetaryl.

Conclusion

All claims except claims 24 and 27 were indicated as substantively allowable. As it has been demonstrated that claim 24 and claim 27 dependent thereon are actually free of the art, applicants respectfully submit that pending and examined claims 10-12, 14 and 21-30 are in a position for allowance and respectfully request that withdrawn claims 15-20 be rejoined and passed to issue as well.

Should other small issues arise that could be settled over the phone, a telephone call to the undersigned is respectfully requested.

In the unlikely event that the transmittal letter is separated from this document and the Patent Office determines that an extension and/or other relief is required, applicants petition for any required relief including extensions of time and authorize the Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952** referencing docket No. 415852000200.

Dated: January 20, 2011

Respectfully submitted,

Electronic signature: / Kate H. Murashige /

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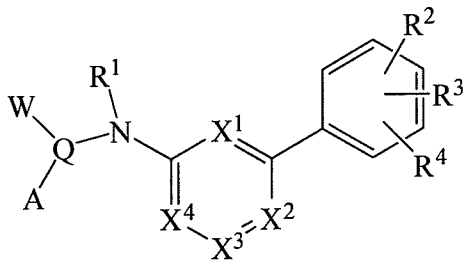
Currently Pending Claims

10. A compound of the formula (V)



(V) to claim 24

or a pharmaceutically acceptable salt, enantiomer, or diastereomer form thereof;

wherein X^1 and X^2 are N and X^3 and X^4 are C independently substituted with Y;

R^1 is H, C_{1-6} alkyl, C_{1-6} alkylNR^5R^6, C_{1-6} alkylNR^5COR^6, C_{1-6} alkyl$NR^5SO_2R^6$, C_{1-6} alkylCO_2R^5, or C_{1-6} alkyl$CONR^5R^6$,

wherein R^5 and R^6 are each independently H, C_{1-4} alkyl, aryl, hetaryl, C_{1-4} alkylaryl, or C_{1-4} alkylhetaryl or may be joined to form a 3-8 membered ring optionally containing one of O, S or NR^7;

wherein R^7 is H or C_{1-4} alkyl;

R^2 is selected from OH, C_{1-6} alkylOH, OC_{2-6} alkylOH, C_{1-6} alkylNR^8R^9, OC_{2-6} alkylNR^8R^9, C_{1-6} alkylNR^8COR^9, OC_{2-6} alkylNR^8COR^9, C_{1-6} alkylhetaryl, OC_{2-6} alkylhetaryl, $OCONR^8R^9$, NR^8COOR^9, $NR^{10}CONR^8R^9$, $CONR^8R^9$, and NR^8COR^{12};

wherein R^8 and R^9 are each independently H, C_{1-4} alkyl, C_{1-4} alkyl$NR^{11}R^{13}$, hetaryl, or cyclohetalkyl, or may be joined to form a 3-8 membered ring optionally containing one of O, S or NR^{14};

wherein R^{12} is C_{2-4} alkyl, C_{1-4} alkyl$NR^{11}R^{13}$, hetaryl, or cyclohetalkyl; to claim 24

wherein R^{11} and R^{13} are each independently H, or C_{1-4} alkyl, or may be joined to form a 3-8 membered ring optionally containing one of O, S or NR^{14};

wherein R^{14} is H or C_{1-4} alkyl;

wherein R^{10} is H or C_{1-4} alkyl;

R^3 and R^4 are each independently H, halogen, C_{1-4} alkyl, OH, OC_{1-4} alkyl, CF_3, or OCF_3;

Q is C_{1-4} alkyl;

W is selected from C_{1-4} alkyl, and C_{2-6} alkenyl; where C_{1-4} alkyl or C_{2-6} alkenyl may be optionally substituted with C_{1-4} alkyl, OH, OC_{1-4} alkyl, or $NR^{15}R^{16}$;

wherein R^{15}, and R^{16} are each independently H, C_{1-4} alkyl, C_{1-4} alkyl cycloalkyl, C_{1-4} alkyl cyclohetalkyl, aryl, or hetaryl, or may be joined to form a 3-8 membered ring optionally containing one of O, S or NR^{17};

wherein R^{17} is H, or C_{1-4} alkyl;

A is aryl or hetaryl optionally substituted with 0-3 substituents independently selected from halogen, C_{1-4} alkyl, CF_3, aryl, hetaryl, OCF_3, OC_{1-4} alkyl, OC_{2-5} alkyl$NR^{18}R^{19}$, Oaryl, Ohetaryl, CO_2R^{18}, $CONR^{18}R^{19}$, $NR^{18}R^{19}$, C_{1-4} alkyl$NR^{18}R^{19}$, $NR^{20}C_{1-4}$ alkyl$NR^{18}R^{19}$, $NR^{18}COR^{19}$, $NR^{20}CONR^{18}R^{19}$, and $NR^{18}SO_2R^{19}$;

wherein R^{18} and R^{19} are each independently H, C_{1-4} alkyl, C_{1-4} alkyl cyclohetalkyl, aryl, hetaryl, C_{1-4} alkyl aryl, or C_{1-4} alkyl hetaryl, or may be joined to form a 3-8 membered ring optionally containing one of O, S or NR^{21};

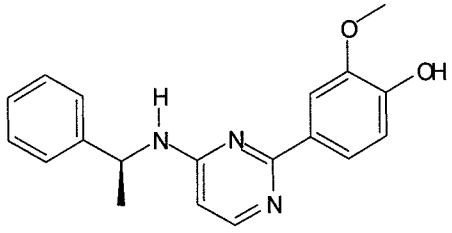
wherein R^{21} is H or C_{1-4} alkyl; to claim 24

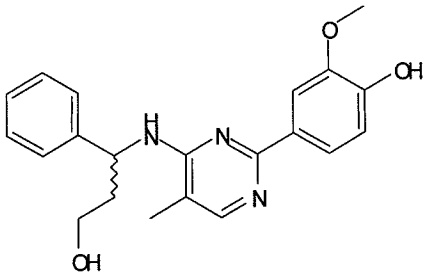
wherein R^{20} is H or C_{1-4} alkyl;

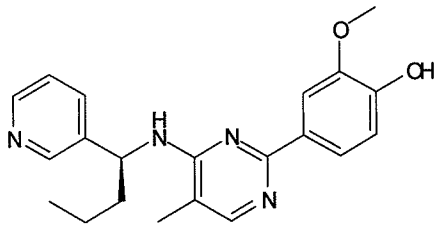
Y is selected from H, C_{1-4} alkyl, OH, and $NR^{22}R^{23}$;

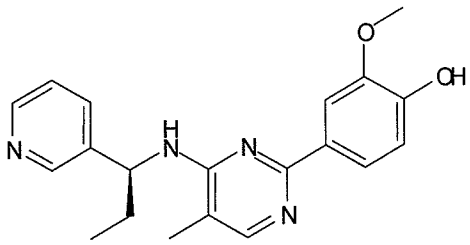
wherein R^{22}, R^{23} are each independently H or C_{1-4} alkyl. to claim 24

11. A compound according to claim 10 selected from the group consisting of:





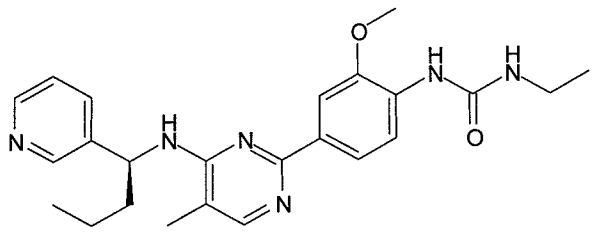




and

or a pharmaceutically acceptable salt or enantiomer form thereof.

12. A compound of the formula:



or a pharmaceutically acceptable salt or enantiomer form thereof.

14. A composition comprising a carrier and at least one compound according to claim 10.

21. A composition comprising a carrier and at least one compound according to claim 11.

22. A composition comprising a carrier and at least one compound according to claim 12.

23. The compound of claim 10, wherein R^2 is selected from C_{1-6} alkylOH, OC_{2-6} alkylOH, C_{1-6} alkylNR^8R^9, OC_{2-6} alkylNR^8R^9, C_{1-6} alkylNR^8COR^9, OC_{2-6} alkylNR^8COR^9, C_{1-6} alkylhetaryl, OC_{2-6} alkylhetaryl, $OCONR^8R^9$, NR^8COOR^9, $NR^{10}CONR^8R^9$, $CONR^8R^9$, and NR^8COR^{12}.

24. The compound of claim 23, wherein: As allowed except for dependence

R^1 is H, C_{1-6} alkyl, C_{1-6} alkylNR^5R^6, where R^5 and R^6 are each independently H, C_{1-4} alkyl, aryl, or hetaryl, or may be joined to form a 3-8 membered ring optionally containing one of O, S or NR^7;

wherein R^7 is H or C_{1-4} alkyl;

Q is CH;

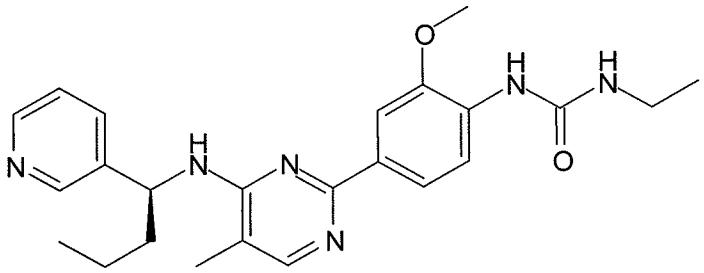
W is C_{1-4} alkyl, or C_{2-6} alkenyl; where C_{1-4} alkyl or C_{2-6} alkenyl may be optionally substituted with C_{1-4} alkyl, OH, OC_{1-4} alkyl or $NR^{15}R^{16}$;

R^{15}, and R^{16} are each independently H or C_{1-4} alkyl, or may be joined to form a 3-8 membered ring optionally containing one of O, S or NR^{17};

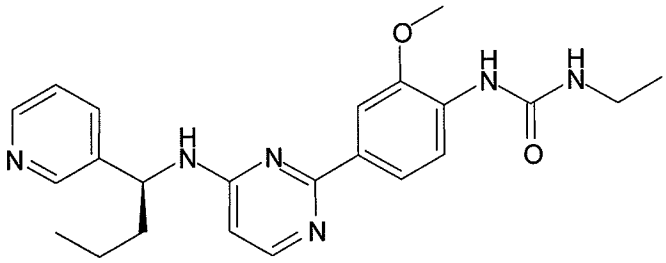
A is aryl, or hetaryl optionally substituted with 0-2 substituents independently selected from halogen, C_{1-4} alkyl, CF_3, aryl, hetaryl, OCF_3, OC_{1-4} alkyl, OC_{2-5} alkyl$NR^{18}R^{19}$, Oaryl, Ohetaryl, CO_2R^{18}, $CONR^{18}R^{19}$, $NR^{18}R^{19}$, C_{1-4} alkyl$NR^{18}R^{19}$, $NR^{20}C_{1-4}$ alkyl$NR^{18}R^{19}$, $NR^{18}COR^{19}$, $NR^{20}CONR^{18}R^{19}$, and $NR^{18}SO_2R^{19}$; and

Y is selected from H, C_{1-4} alkyl and $NR^{22}R^{23}$.

25. The compound of claim 23 selected from:



and



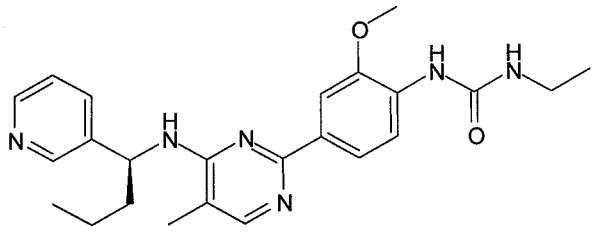
or a pharmaceutically acceptable salt or enantiomer form thereof.

26. A composition comprising a carrier and at least one compound according to claim 23.

27. A composition comprising a carrier and at least one compound according to claim 24.

28. A composition comprising a carrier and at least one compound according to claim 25.

29. A compound of the formula:



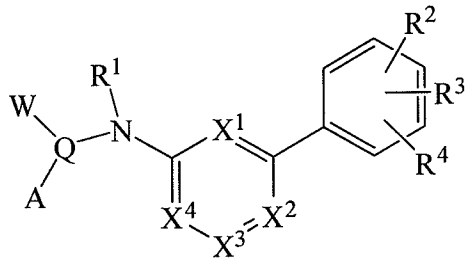
30. A composition comprising a carrier and at least one compound according to claim 29.

21. A composition comprising a carrier and at least one compound according to claim 11.

22. A composition comprising a carrier and at least one compound according to claim 12.

23. The tubulin inhibitor of claim 10, wherein R^2 is selected from C_{1-6} alkylOH, OC_{2-6} alkylOH, C_{1-6} alkylNR^8R^9, OC_{2-6} alkylNR^8R^9, C_{1-6} alkylNR^8COR^9, OC_{2-6} alkylNR^8COR^9, C_{1-6} alkylhetaryl, OC_{2-6} alkylhetaryl, $OCONR^8R^9$, NR^8COOR^9, $NR^{10}CONR^8R^9$, $CONR^8R^9$, and NR^8COR^{12}.

24. A compound of the formula (V)



(V)

from claim 10

or a pharmaceutically acceptable salt, enantiomer, or diastereomer form thereof;

wherein X^1 and X^2 are N and X^3 and X^4 are C independently substituted with Y; wherein:

R^1 is H, C_{1-6} alkyl, C_{1-6} alkylNR^5R^6, where R^5 and R^6 are each independently H, C_{1-4} alkyl, aryl, or hetaryl, or may be joined to form a 3-8 membered ring optionally containing one of O, S or NR^7;

in claim 24 originally

wherein R^7 is H or C_{1-4} alkyl;

R^2 is selected from C_{1-6} alkylOH, OC_{2-6} alkylOH, C_{1-6} alkylNR^8R^9, OC_{2-6} alkylNR^8R^9, C_{1-6} alkylNR^8COR^9, OC_{2-6} alkylNR^8COR^9, C_{1-6} alkylhetaryl, OC_{2-6} alkylhetaryl, $OCONR^8R^9$, NR^8COOR^9, $NR^{10}CONR^8R^9$, $CONR^8R^9$, and NR^8COR^{12};

from claim 23

wherein R^8 and R^9 are each independently H, C_{1-4} alkyl, C_{1-4} alkyl$NR^{11}R^{13}$, hetaryl, or cyclohetalkyl, or may be joined to form a 3-8 membered ring optionally containing one of O, S or NR^{14};

from claim 10

wherein R^{12} is C_{2-4} alkyl, C_{1-4} alkyl$NR^{11}R^{13}$, hetaryl, or cyclohetalkyl;

wherein R^{11} and R^{13} are each independently H, or C_{1-4} alkyl, or may be joined to form a 3-8 membered ring optionally containing one of O, S or NR^{14};

wherein R^{14} is H or C_{1-4} alkyl;

wherein R^{10} is H or C_{1-4} alkyl; from cl 10

R^3 and R^4 are each independently H, halogen, C_{1-4} alkyl, OH, OC_{1-4} alkyl, CF_3, or OCF_3;

Q is CH;

W is C_{1-4} alkyl, or C_{2-6} alkenyl; where C_{1-4} alkyl or C_{2-6} alkenyl may be optionally substituted with C_{1-4} alkyl, OH, OC_{1-4} alkyl or $NR^{15}R^{16}$;

R^{15}, and R^{16} are each independently H or C_{1-4} alkyl, or may be joined to form a 3-8 membered ring optionally containing one of O, S or NR^{17}; in claim 24 orig.

A is aryl, or hetaryl optionally substituted with 0-2 substituents independently selected from halogen, C_{1-4} alkyl, CF_3, aryl, hetaryl, OCF_3, OC_{1-4} alkyl, OC_{2-5} alkyl$NR^{18}R^{19}$, Oaryl, Ohetaryl, CO_2R^{18}, $CONR^{18}R^{19}$, $NR^{18}R^{19}$, C_{1-4} alkyl$NR^{18}R^{19}$, $NR^{20}C_{1-4}$ alkyl$NR^{18}R^{19}$, $NR^{18}COR^{19}$, $NR^{20}CONR^{18}R^{19}$, and $NR^{18}SO_2R^{19}$;

wherein R^{18} and R^{19} are each independently H, C_{1-4} alkyl, C_{1-4} alkyl cyclohetalkyl, aryl, hetaryl, C_{1-4} alkyl aryl, or C_{1-4} alkyl hetaryl, or may be joined to form a 3-8 membered ring optionally containing one of O, S or NR^{21};

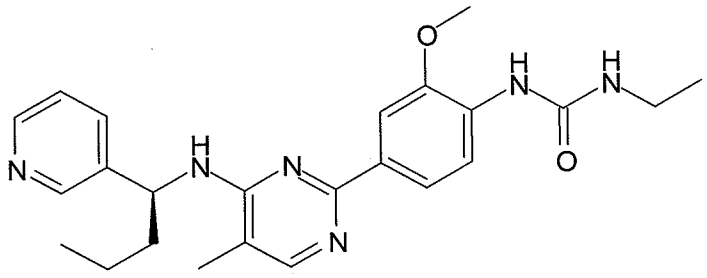
wherein R^{21} is H or C_{1-4} alkyl; from claim 10

wherein R^{20} is H or C_{1-4} alkyl;

Y is selected from H, C_{1-4} alkyl and $NR^{22}R^{23}$; in cl 24 orig

wherein R^{22} R^{23} are each independently H or C_{1-4} alkyl. from claim 10

25. The compound of claim 24 selected from:



and